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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,021	09/16/2003	Mary Kay Delmedico	TRM-001	5500
20583	7590	06/06/2007		EXAMINER
JONES DAY				PARKIN, JEFFREY S
222 EAST 41ST ST			ART UNIT	PAPER NUMBER
NEW YORK, NY 10017			1648	
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			06/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/664,021	DELMEDICO ET AL.
	Examiner	Art Unit
	Jeffrey S. Parkin, Ph.D.	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 05 March 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-71 and 76-87 is/are pending in the application.
 - 4a) Of the above claim(s) 53-71 and 76-79 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-52, 80-87 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 09/16/03; 08/06/04.
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) Notice of Informal Patent Application
- 6) Other: Notice to Comply...

Notice to Comply	Application No. 10/664,021	Applicant(s) Delmedico, M. K., et al.	
	Examiner Jeffrey S. Parkin	Art Unit 1648	Paper No. 05/29/2007

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- 7. Other: Applicants are reminded that sequences appearing in the specification and/or drawings must be identified by a sequence identifier (SEQ ID NO.:) in accordance with 37 C.F.R. 1.821(d). Sequence identifiers for sequences appearing in the drawings may appear in the Brief Description of the Drawings. Applicant must provide appropriate amendments to the specification and/or drawings inserting the required sequence identifiers. Extensive amendments may necessitate the submission of a substitute specification and drawings.

Applicant May Need to Provide:

- An substitute computer readable form (CRF) copy of the "Sequence Listing".
- An substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

- For Rules Interpretation, call (571) 272-0951
- For Patentin Software Program Help, call Patent EBC at 1-866-217-9197 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.
- Send e-mail correspondence for Patentin Software Program Help @ ebc@uspto.gov.

To Download Patentin Software, visit <http://www.uspto.gov/web/patents/software.htm>.

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

Serial No.: 10/664,021

Docket No.: N/A

Applicants: Delmedico, M. K., and J. Dwyer

Filing Date: 09/16/2003

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 05 March, 2007. Claims 1-71 and 76-87 are pending in the instant application. Newly submitted claims 84-87 are directed to an invention that is independent or distinct from the invention originally claimed. The claims are directed toward methods of inhibiting HIV infection by administering polypeptides capable of forming trimeric structures. These claims would be encompassed by Group II as set forth in the original restriction requirement. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 84-87 are withdrawn from further consideration as being directed towards a nonelected invention (refer to 37 C.F.R. § 1.142(b) and M.P.E.P. § 821.03). Thus, the claims can be summarized as follows: Claims 1-52 and 80-83 are currently under examination and claims 53-71, 76-79, and 84-87 are withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

37 C.F.R. § 1.98

Applicants are reminded that the listing of references in the specification is not a proper information disclosure statement. 37 C.F.R. § 1.98(b) requires a list of all patents, publications, applications, or other information submitted for consideration by the Office, and M.P.E.P. § 609.04(a),

subsection I. states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

37 C.F.R. § 1.821

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicants are reminded that sequences appearing in the specification and/or **drawings** (see Figures 1-3) must be identified by a sequence identifier (SEQ ID NO.:) in accordance with 37 C.F.R. § 1.821(d). Sequence identifiers for sequences appearing in the drawings may appear in the Brief Description of the Drawings. Applicant must provide appropriate amendments to the specification and/or drawings inserting the required sequence identifiers. Extensive amendments may necessitate the submission of a substitute specification.

35 U.S.C. § 112, Second Paragraph

Claims 1-36, 38, 40, 41, 43-50, 52, 80-83 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard

as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

First, the reference to a "native" amino acid sequence in claims 1, 21, 29, 41, 43, 45, 47, 49, and 80 is confusing. Clinical viral isolates, including those from the same patient, will display considerable phenotypic variability, yet these could all be termed "native" sequences. Thus, the term "native" as it is applied here is not further limiting since it clearly fails to set forth any meaningful structural criteria. Applicants may wish to amend the claim language to simply recite a synthetic HR1 peptide consisting or SEQ ID NO.: 1, or a synthetic HR1 peptide consisting of one of the amino acid sequences set forth in Figure 2. Alternatively, applicants could provide a reference isolate (i.e., a synthetic HR1 peptide consisting of amino acids 543-600 of the envelope glycoprotein, wherein said numbering scheme is based upon HIV-1 isolate IIIB; or a one of the naturally occurring isolates set forth in Figure 2).

Second, claims 4, 29, 47, 49, is confusing because it it initially references the heptadic repeat "efgabcdef", but then references different "C-terminal" positions. Any given polypeptide only has a single C-terminus. Thus, it is not readily manifest if the claims are directed toward an amino acid in a C-terminal heptadic repeat (i.e., NH2-X-abcdefgabcdefgabcdefgabcd-efg**abcdefg**-COOH) or individual amino acids located in truncated heptadic repeats (i.e., NH2-X-abcdefgabcdefgabcdefgabcde-COOH; NH2-X-abcdefgabcdefgabcde-**abcdefgabcdefgabcdef**-COOH). Appropriate correction is required.

Third, claims 6-10, 12, 14, 16, 18, 20, 23, 24, 26, 28, 31, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 81, and 83 are vague

and indefinite for referencing "one or more reactive functionalities" and an "amino acid substitution comprising an addition". The first term is vague and indefinite since it fails to set forth any meaningful structural limitations. Although the term is defined in the specification (see page 8), nevertheless, applicants are reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *In re Van Geuns*, 988 F.2d 1181, 26 U.S.P.Q.2d 1057 (Fed. Cir. 1993). Applicants may obviate the rejection by amending the claim language to more clearly set forth the structure of the "reactive functionality". For instance, the second term is confusing because an amino acid substitution does not consist of adding additional amino acids to the protein. It consists of replacing one or more amino acids with another.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 4, 11, 17, 29, 33, 41, 47, 49, 80, and 82 are rejected under 35 U.S.C. § 102(a) as being anticipated by Bewley et al. (2002). This teaching discloses synthetic peptides derived from the HR1 region of HIV-1 gp41 with potent antiviral activity. The peptides further comprised one or more amino acid

substitutions, including the designated heptadic positions (i.e., "e" or "f"). It was also demonstrated that these polypeptides form trimeric structures in solution. Therefore, this teaching meets all of the claimed limitations.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 3, 5-10, 12-16, 18-28, 30-32, 34-40, 42-46, 48, 50-52, 81, and 83, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bewley et al. (2002) in view of Barney et al. (1999). As set forth *supra*, Bewley and colleagues disclose synthetic peptides derived from the HR1 region of HIV-1 gp41 with potent antiviral activity. The peptides further comprised one or more amino acid substitutions, including the designated heptadic positions (i.e., "e" or "f"). It was also demonstrated that these polypeptides form trimeric structures in solution. This teaching does not provide mutations in other regions of the heptadic repeat (i.e., "a", "d", or "b") or various modifications to the polypeptide (i.e., the addition of reactive groups or carriers). However, Barney and associates provide similar polypeptides with enhanced pharmacokinetic properties. Therefore, it would have been *prima facie* obvious to one of

ordinary skill in the art at the time of the invention to modify the synthetic peptides of Bewley et al. (2002), as described by Barney et al. (1999), since this would produce synthetic polypeptides with enhanced pharmacokinetic profiles. Moreover, one of ordinary skill in the art would have been motivated to make "conservative" substitutions in other portions of the heptadic repeat (i.e., "a", "d", or "b") since structurally similar polypeptides would reasonably be expected to have similar activities.

Applicants are reminded that a *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. See M.P.E.P. 2144.09. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 U.S.P.Q. 245, 254 (C.C.P.A. 1979). See *In re Papesch*, 315 F.2d 384, 137 U.S.P.Q. 43 (C.C.P.A. 1963) (discussed in more detail below) and *In re Dillon*, 919 F.2d 688, 16 U.S.P.Q.2d 1897 (Fed. Cir. 1991) (discussed below and in M.P.E.P. § 2144) for an extensive review of the case law pertaining to obviousness based on close structural similarity of chemical compounds. See also M.P.E.P. § 2144.08, paragraph II.A.4.(c). Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH₂- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 U.S.P.Q. 426

(C.C.P.A. 1977). See also *In re May*, 574 F.2d 1082, 197 U.S.P.Q. 601 (C.C.P.A. 1978) (stereoisomers *prima facie* obvious).

Claims 1-52 and 80-83 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chan *et al.* (1997) in view of Barney *et al.* (1999). Chan and colleagues disclose synthetic peptides derived from the HR1 region of HIV-1 gp41 with potent antiviral activity. This teaching does not provide mutations in other regions of the heptadic repeat (i.e., "a", "c", "d", or "b") or various modifications to the polypeptide (i.e., the addition of reactive groups or carriers). However, Barney and associates provide similar polypeptides with enhanced pharmacokinetic properties. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the synthetic peptides of Chan *et al.* (1997), as described by Barney *et al.* (1999), since this would produce synthetic polypeptides with enhanced pharmacokinetic profiles. Moreover, one of ordinary skill in the art would have been motivated to make "conservative" substitutions in other portions of the heptadic repeat (i.e., "a", "c", "d", or "b") since structurally similar polypeptides would reasonably be expected to have similar activities.

Applicants are reminded that a *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. See M.P.E.P. 2144.09. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313,

203 U.S.P.Q. 245, 254 (C.C.P.A. 1979). See *In re Papesch*, 315 F.2d 381, 137 U.S.P.Q. 43 (C.C.P.A. 1963) (discussed in more detail below) and *In re Dillon*, 919 F.2d 688, 16 U.S.P.Q.2d 1897 (Fed. Cir. 1991) (discussed below and in M.P.E.P. § 2144) for an extensive review of the case law pertaining to obviousness based on close structural similarity of chemical compounds. See also M.P.E.P. § 2144.08, paragraph II.A.4.(c). Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH₂- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 U.S.P.Q. 426 (C.C.P.A. 1977). See also *In re May*, 574 F.2d 1082, 197 U.S.P.Q. 601 (C.C.P.A. 1978) (stereoisomers *prima facie* obvious).

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

The previous rejection of claims 1-36, 41-50, and 52 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is hereby withdrawn in response to applicants' arguments.

Scope of Enablement

Claims 1-36, 40-52, and 80-83 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims encompass a large genus of polypeptides comprising an inordinate number of variants (i.e., at positions "a", "b", "c", "e", "f", etc.). The variants are not limited to "conservative" amino acid substitutions and encompass all naturally-occurring amino acids. Appropriately drafted claim language directed toward those specific variants with the desired activity would be acceptable. However, the disclosure does not support the full breadth of the claim coverage desired.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of

the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

Amount of Direction/Guidance Provided

The disclosure fails to provide adequate guidance pertaining to those regions of the heptadic repeat that can tolerate amino acid substitutions and still retain all the desired activities (i.e., trimer formation; antiviral activity). The disclosure also fails to provide sufficient guidance pertaining to those amino acids that can be readily used to substitute for the parent amino acid.

Claim Breadth

The claim breadth encompasses an inordinate number of species. The claims only limit the peptide of interest to between 14 and 60 amino acid residues. The claims allow for amino acid substitutions throughout the heptadic repeat without providing any meaningful structural guidance.

Working Examples

The specification only provides a limited number of working examples which are insufficient to enable the full breadth of the claim language desired.

Unpredictability of the Art

It is readily manifest from the art that the skilled artisan cannot make amino acid substitutions, including conservative substitutions, anywhere throughout the peptide of interest. It is important that the peptide retain its ability to form a trimeric coiled-coil structure. Studies have shown that even conservative amino acid substitutions can abrogate peptide activity (Lu et al., 2001; Bewley et al., 2002). The disclosure

fails to provide sufficient guidance pertaining to those amino acid substitutions that are permissible.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skill artisan to practice the claimed invention.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

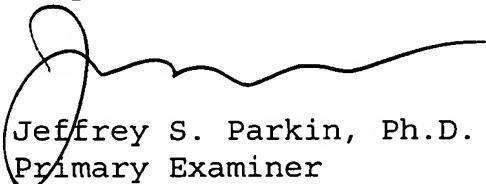
Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system,

U.S. Serial No.: 10/664,021
Applicants: Delmedico, M .K., and J. Dwyer

see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,



Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

29 May, 2007